REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

I. Status of the Claims

Claims 1-7, 15-19 and 21-28 were pending and under active consideration in the subject application. With this submission no claims have been amended, no claims have been canceled and no claims have been newly added. Hence, upon entry of this paper, claims 1-7, 15-19 and 21-28 will remain pending and under active consideration.

A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

II. 35 U.S.C. §112 Rejection

Claims 26 and 27 are rejected under 35 U.S.C. §112 as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner alleges that claims 26 and 27 of the claimed invention are indefinite for reciting the term "gene." Examiner alleges that the nucleic acid sequences encoding the anti-HM1.24 antibody appear limited to the specific coding regions, and do not include expression control elements that fall under the definition of a gene.

Applicants respectfully submit that one of ordinary skill in the art would recognize what gene encodes the anti-HM1.24 antibody. This is true especially in light of the fact that applicants have deposited the hybridoma FERM BP-5233 as the hybridoma that generates this antibody. As such, applicants respectfully request withdrawal of the subject rejection.

III. 35 U.S.C. §112 Rejection

Claims 24-28 are rejected under 35 U.S.C. §112 as allegedly not enabled because the "specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; [or] (2) reproducible from the written description."

Applicants now submit a deposit statement stating that the deposited hybridoma has been accepted by an International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposited material will be irrevocably removed upon the grant of a patent on this application. As such, the rejection should be rendered moot. Applicants thus respectfully request the rejection be withdrawn.

IV. 35 U.S.C. §102 Rejection

Claims 15-19, 21, and 22 are rejected under 35 U.S.C. §102 as allegedly anticipated by Morin. Specifically, the Office states that objective evidence must be "factually supported by an appropriate affidavit or declaration to be of probative value includes evidence of...inoperability of the prior art..." (Office action, page 8). Applicants have enabled the use of specific anti-HM1.24 antibodies to treat a disease, while Morin has not. Additionally, Morin has not disclosed the relationship between expression of BST-2 antigen protein and the disease state. Applicants now include a declaration under 37 CFR §1.132 to support traversal of the 35 U.S.C. §102 rejection. Thus, Applicants respectfully request reconsideration and withdrawal of the rejection.

A. The Current Enablement Standard

Neither the accidental, unappreciated occurrence of a product or process in the prior art, nor the speculative listing of a product (such as a chemical compound) as part of a large number of possible occurrences is an anticipation. *In re Wiggins*, 488 F.2d 538, 179 U.S.P.Q,. 421 (CCPA 1973). The court in *Wiggins*, held that the rejection of appellants' claims under 35 U.S.C. §102(b), based upon a previously published article, was improper since the article itself did not disclose all that was necessary to put the compounds in the hands of the public. The court continued that the compounds listed in the article constituted nothing more than speculation, and therefore did not mandate a rejection of appellants' claims.

The specification and drawings must provide sufficient information about the invention so as "to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same." 35 U.S.C. §112. A specification disclosure is not enabling if unreasonable experimentation is required. *In re Gardner*, 427

F.2d 786, 166 USPQ 138 (CCPA 1970). In the instant case, the one line reference in Morin is speculation regarding a possible future use and does not enable one of ordinary skill in the art to practice the invention.

B. Morin Does Not Enable the Use of Anti-BST-2 Antibody to Treat Ovarian Cancer

The Morin reference refers to treatment of ovarian cancer by an anti-BST-2 antibody. However, this reference is speculative and is part of a long list (at least 39) of other tumor cell markers. The Morin reference does not provide experimental proof that ovarian cancer can be treated by an anti-BST-2 antibody. As recited in the attached 1.132 declaration, "[n]owhere in the specification does Morin teach how to use or generate specific anti-HM1.24 antibodies to treat a disease. Additionally, Morin does not provide experimental proof that ovarian cancer can be treated by an anti-BST-2 antibody." (See Koishihara declaration, page 2) Thus, the Morin reference is simply a speculative listing of a product as part of a large number of possible occurrences, and cannot be the basis for an anticipation. See *Wiggins*.

C. Morin Does Not Disclose Specific Anti-HM1.24 Antibodies

In the Morin reference, **no antibodies were in fact prepared**. (See Koishihara declaration, page 2) Therefore the concrete use of anti-BST-2 antibody would not be clear to a person with ordinary skill in the art. Specifically, Morin does not disclose the use of anti-HM1.24 antibodies. (See Koishihara declaration, page 2.) Morin simply lists a large number of possible occurrences, which cannot support an anticipation rejection. See *Wiggins*. Morin does not give a concrete example or specific examples to use or carry out the claimed invention. Thus, the Morin reference simply constitutes mere speculation.

D. Morin Does Not Address the Discrepancy Between mRNA Levels and Protein Levels

In addition, there is a discrepancy between mRNA levels and protein expression levels. The Morin reference only shows that mRNA levels are increased in ovarian tumor cells, and does not show that protein levels are increased. As shown below, this is not a trivial distinction.

Antibodies used to treat cancers are most effective if differentially expressed in cancer cells **at the protein level**. (See Koishihara declaration, page 2) Morin does not teach the correlation between mRNA BST-2 levels and protein expression levels of BST-2. (See Koishihara declaration, page 2.) This is important because post-transcriptional regulation could play a key role in protein regulation. Specifically, in cancer cells, increases in mRNA levels do not always correlate to increases in protein expression levels. (See Koishihara declaration, page 3.) Thus, from the Morin reference, one of ordinary skill in the art would not necessarily focus on generating BST-2 antibodies to treat cancer. (See Koishihara declaration, page 3.)

Several authors have shown that the discrepancy between mRNA levels and protein levels can play a crucial role in tumor progression. (See Koishihara declaration, page 3.) Specifically, Roppen *et al. J. Clin. Pathol* (2001), 54: 533-538 states "Together with reduced AP-2γ expression in high grade carcinomas, this might contribute to tumor progression. The discrepancy between mRNA and protein expression suggests that posttranscriptional regulatory mechanism might modify the availability of functional AP-2γ protein in colorectal carcinoma." Additionally, Fujimoto *et al.*, *Jpn. J. Electroph.* (1996), 40:313 25-29 states "A discrepancy between results of nm 23-H1 protein level by Western blot and mRNA level by Northern blot was observed in HCCs," and that "These data suggest that the expression of nm 23-H1 was mainly regulated at a post-transcriptional level." Taken together these references show that protein levels are not always correlated with mRNA levels in tumors. (See Koishihara declaration, page 3.)

The Morin reference, in Examples, confirms only that an amount of mRNA for a plurality of genes expressed was increased in ovarian tumor cells. Due to the discrepancy between mRNA level and protein level, it is not clear, and not described that a large amount of BST-2 protein is translated.

As Morin does not recite every element of the current claims it may not serve as a proper anticipatory reference. In addition, Applicants note that Morin does not describe or suggest the use of an anti-HM1.24 antibody having ADCC activity.

E. Conclusion

The Morin reference is not enabling, and thus cannot be used as an anticipation reference.

Additionally, the present inventors found, for the first time, that BST-2 (HM1.24) antigen is expressed at the protein level in solid cancers including ovarian cancer. In addition, the present inventors found, for the first time, that an anti-HM1.24 antibody has ADCC activity against solid cancers, and thereby discovered the presently claimed invention for treatment of solid cancers using an anti-HM1.24 antibody.

In conclusion, (1) although the Morin reference describes that a plurality of genes (at the mRNA level) such as BST-2 are expressed in ovarian tumor and therefore can be used as a marker for ovarian tumor, (2) expression of the BST-2 antigen protein is not clear in the Morin reference, and (3) no antibody was prepared in the Morin reference. Thus, a concrete therapeutic use of BST-2 could not have been predicted based on this reference. Furthermore, the Morin reference does not disclose the present invention for treatment of an ovarian tumor using anti-BST-2 (HM1.24) antibody.

CONCLUSION

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing or a credit card payment form being unsigned, providing incorrect information resulting in a rejected credit card transaction, or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date July 14, 2009 By _____

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